

§Appl. No. 09/996,956
Amdt. dated July 1, 2004
Reply to Office Action of, April 1, 2004

REMARKS

Entry of the attached amendment is respectfully requested. Applicant is making a sincere effort to reduce the issues on appeal.

In particular, the claims have been amended to recite "having 100% complementarity thereto." This amendment does not change the scope of the claims since this was always the intended scope that the skilled worker would have understood.

Support for this amendment can be found throughout the specification, e.g., on Page 8, about line 10. Applicant is simply claiming the reverse complement to SEQ ID NO:1. See, e.g., Specification, Page 13 for a disclosure of reverse or antisense sequences. This concept is well understood in the art. For example, a DNA molecule can be comprised of two strands, where each strand is "complementary" to the other. In support of this fact, attached is an excerpt from *Genes V*, which indicates that the base pairing between nucleotides is referred to as being "complementary," consistent with the term as it is used in the present application.

It is urged that this issue is trivial and formal, and should not be referred to the Board of Appeals for resolution. Therefore, if the examiner feels that the present amendment does not resolve the issue, it is urged that an alternative language be suggested in an Advisory action or by calling the undersigned.

Applicant will address the remaining issues set forth in the Office action in an Appeal brief to be filed in due course.

In view of the above remarks, favorable reconsideration is courteously requested. If there are any remaining issues which could be expedited by a telephone conference, the Examiner is courteously invited to telephone counsel at the number indicated below.

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The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



Richard M. Lebovitz, Reg. No. 37,067
Attorney for Applicant(s)

MILLEN, WHITE, ZELANO
& BRANIGAN, P.C.
Arlington Courthouse Plaza 1, Suite 1400
2200 Clarendon Boulevard
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

Attorney Docket No.: ORIGEN-0034

Date: July 1, 2004

GENES V

Benjamin Lewin

OXFORD UNIVERSITY PRESS
Oxford New York Tokyo
1994

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DNA is a double helix

The observation that the bases are present in different amounts in the DNAs of different species led to the concept that the *sequence of bases is the form in which genetic information is carried*. By the 1950s, the concept of genetic information was common: the twin problems it posed were working out the structure of the nucleic acid, and explaining how a sequence of bases in DNA could represent the sequence of amino acids in a protein.

Three notions converged in the construction of the double helix model for DNA by Watson and Crick in 1953:

- ◆ X-ray diffraction data showed that DNA has the form of a regular helix, making a complete turn every 34Å (3.4 nm), with a diameter of ~20Å (2 nm). Since the distance between adjacent nucleotides is 3.4Å, there must be 10 nucleotides per turn.
- ◆ The density of DNA suggests that the helix must contain two polynucleotide chains. The constant diameter of the helix can be explained if the bases in each chain face inward and are restricted so that a purine is always opposite a pyrimidine, avoiding purine-purine (too thick) or pyrimidine-pyrimidine (too thin) partnerships.
- ◆ Irrespective of the actual amounts of each base, the proportion of G is always the same as the proportion of C in DNA, and the proportion of A is always the same as that of T. Thus the composition of any DNA can be described by the proportion of its bases that is G + C, which ranges from 26% to 74% for different species.

Watson and Crick proposed that the two polynucleotide chains in the double helix associate by *hydrogen bonding between the nitrogenous bases*. Figure 4.10 demonstrates that, in their usual forms, G can hydrogen bond specifically only with

Figure 4.10

Complementary base pairing involves the formation of two hydrogen bonds between A and T, and of three hydrogen bonds between G and C. No other pairs form in DNA.

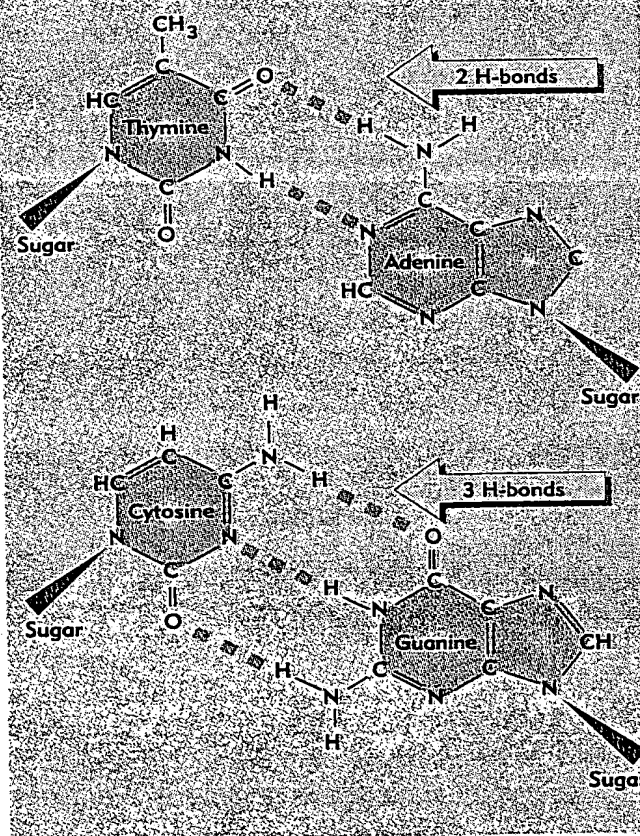
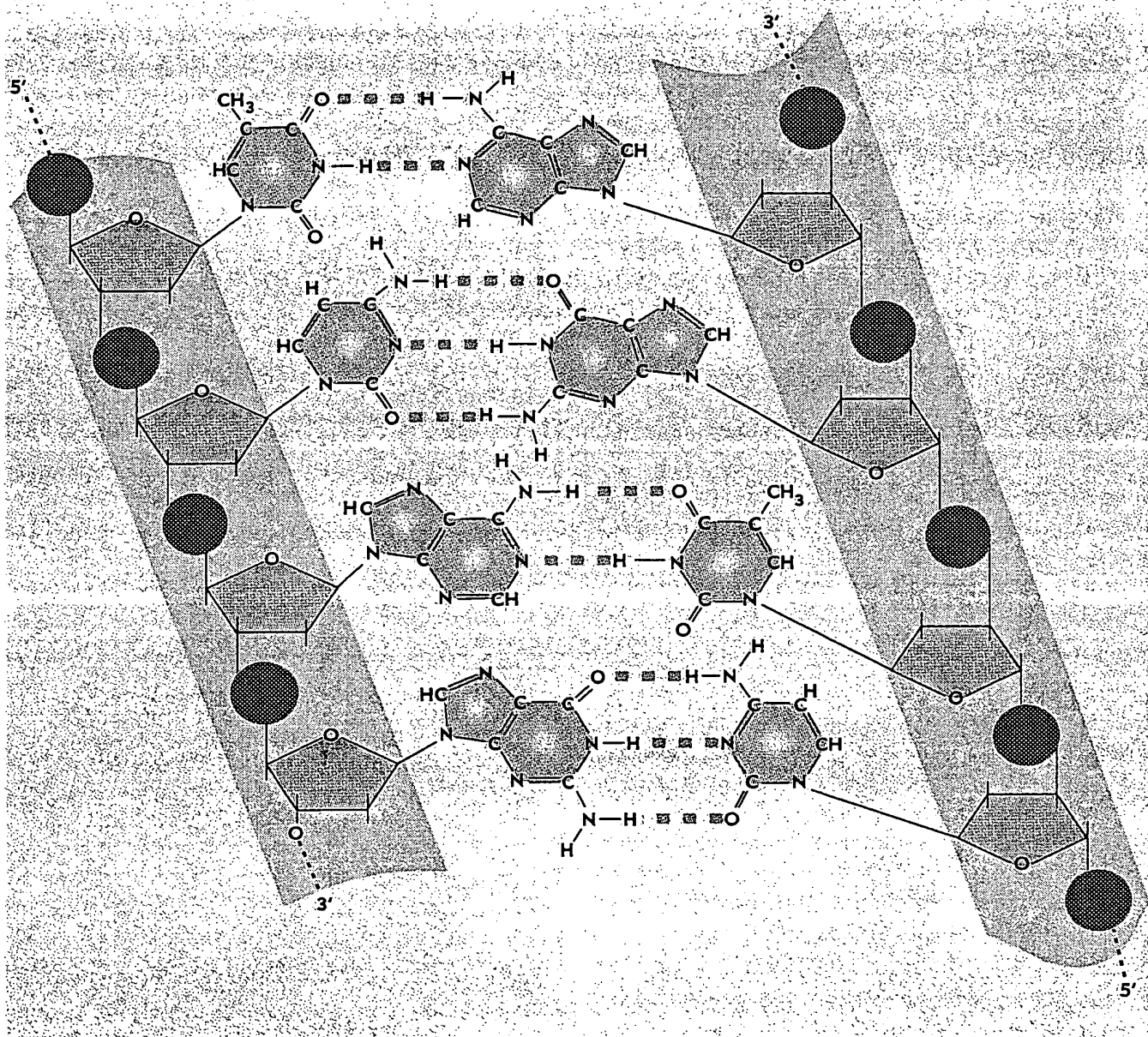


Figure 4.11

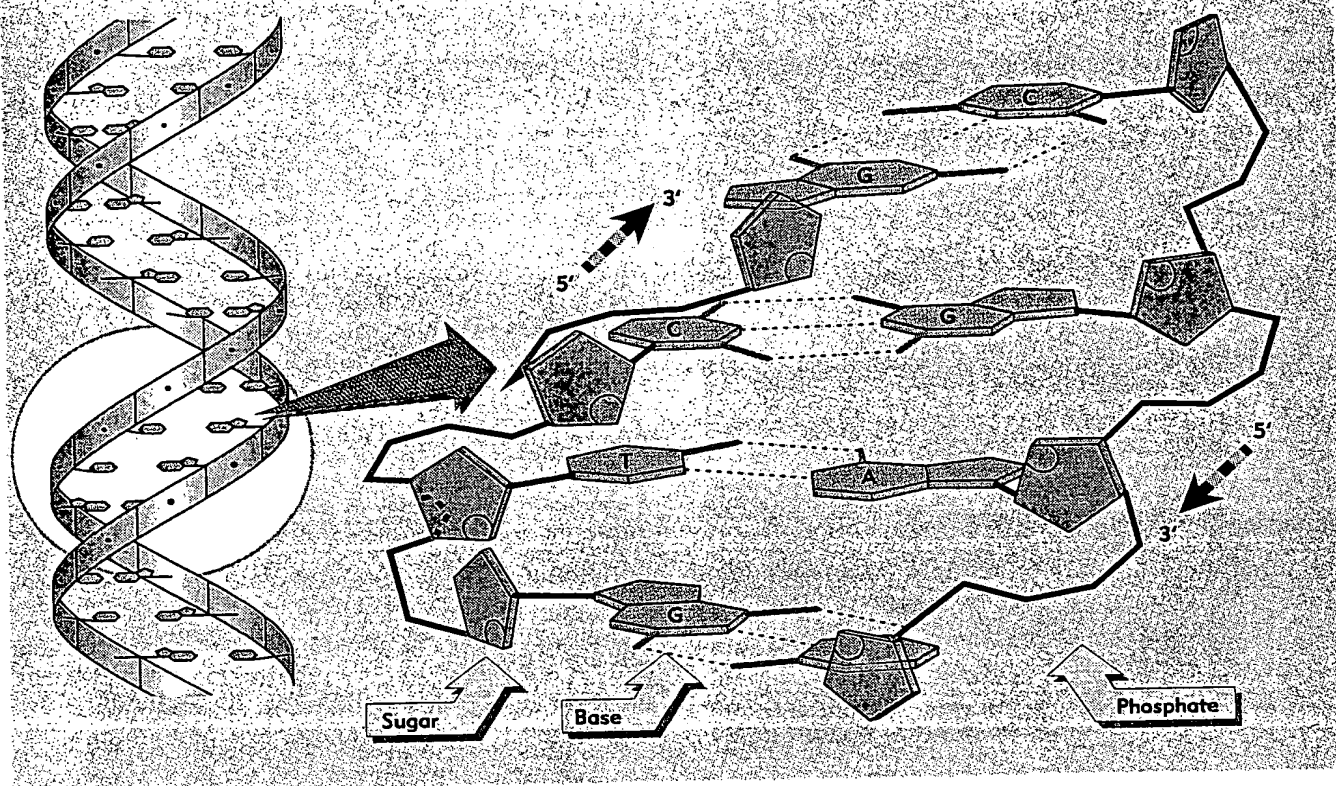
The double helix maintains a constant width because purines always face pyrimidines in the complementary A-T and G-C base pairs.



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Figure 4.12

Flat base pairs lie perpendicular to the sugar-phosphate backbone.



C, while A can bond specifically only with T. These reactions are described as **base pairing**, and the paired bases (G with C, or A with T) are said to be **complementary**.

The model requires the two polynucleotide chains to run in opposite directions (**antiparallel**), as illustrated in Figure 4.11. Looking along the helix, therefore, one strand runs in the 5'-3' direction, while its partner runs 3'-5'.

The sugar-phosphate backbone is on the outside and carries negative charges on the phosphate groups. When DNA is in solution *in vitro*, the charges are neutralized by the binding of metal ions; usually Na^+ is provided. In the natural state *in*

vivo, positively charged proteins provide some of the neutralizing force. These proteins play an important role in determining the organization of DNA in the cell.

The bases lie on the inside. They are flat structures, lying in pairs perpendicular to the axis of the helix. Consider the double helix in terms of a spiral staircase: the base pairs form the treads, as illustrated schematically in Figure 4.12. Proceeding along the helix, bases are stacked above one another, in a sense like a pile of plates.

The base pairs contribute to the thermodynamic stability of the double helix in two ways. Energy is released by the formation of base pairs